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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
KERR, J	
ART UNIT	PAPER NUMBER
1633	18

DATE MAILED: 04/11/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/114,973	Applicant(s) DOVE ET AL.	
	Examiner Janet Kerr	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 January 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *10-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 26-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

Response to Amendment

Applicants' amendment, filed 1/17/01, has been entered.

Claims 26-29 have been added.

Claims 1-29 are pending.

Applicant's election with traverse of Group I in Paper No. 16 is acknowledged. The traversal is on the ground(s) that the examiner has not provided an example of a method of making a transgenic mouse by the claimed technique. This is not persuasive as the mouse is claimed in a product by process format. One skilled in the art of transgenics can readily obtain an animal model of a specific disease and insert a transgene encoding a protein which is thought to be associated in modulating the disease state. It is also argued that Inventions I-III are not independent and distinct. This is not persuasive as the search for each of the inventions is not co-extensive particularly with regard to the literature search. Further, a reference which would anticipate the invention of one group would not necessarily anticipate or even make obvious another group.

The requirement is still deemed proper and is therefore made FINAL.

Claims 10-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 16.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3, 4, 5, 6, 8, 9, and 26 are/remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, and 6 of U.S. Patent No.5,780,236. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method for identifying a segregating mutation at a genetic locus that modifies an index phenotype in a non-human index inbred strain in the instant application encompasses the patented method for identifying a segregating mutation at a murine genetic locus that modifies an index phenotype in an index inbred mouse strain in U.S. Patent No. 5,780,236.

Applicant's arguments filed 4/11/00 have been fully considered but they are not persuasive. It is argued that the methods as claimed in the instant application represent a substantial advance in the effectiveness of the method in terms of reducing the number of animals required, shortening the duration of the method by eliminating entire crosses, and reducing or eliminating possible interfering genetic differences between crossed strains (see applicants' Response, page 7). This is not persuasive as the patented steps and the steps in the claimed invention of the instant application of outcrossing, backcrossing, and verifying that the outlying phenotype is caused by a segregating mutation are the same.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9, and 26-29 are/remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a mouse and a murine genetic locus, does not reasonably provide enablement for any and all non-human animals, and any and all genetic loci. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the reasons of record and the reasons below.

Applicant's arguments filed 4/11/00 have been fully considered but they are not persuasive.

It is argued that all known non-human animals encompassed by the claims strictly follow the rules of genetic inheritance and that it is within the ability of one skilled in the art to utilize the claimed invention with any suitable animal that meets the requirements of the claims (see page 9 of applicants Response). This is not persuasive. As indicated in the Office action of 12/7/99, the specification does not provide sufficient guidance as to what effect the mutagen would have on the genotype and phenotype of any and all non-human animals, or whether the mutation would be preserved through the enabled breeding regimen of the claimed invention such that the method for identifying a segregating mutation would be enabled. In view of the quantity of experimentation necessary to determine the parameters listed above, the lack of direction or guidance provided by the specification, the absence of working examples for the demonstration or correlation to any and all non-human animals and any and all genetic loci, the unpredictable state of the art with respect to genotypic and phenotypic outcomes of all the various possible crossing combinations, and the breadth of the claims to any and all non-human animals, and any and all genetic loci, it would require undue experimentation for one skilled in the art to practice the invention as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 3-6, 8, 9, and 26 are/remain rejected under 35 U.S.C. 102(a) as being anticipated by Bilger *et al.* for the reasons of record, reiterated herein, and the reasons below.

Bilger *et al.* teach a method for identifying a segregating mutation at a genetic locus that modifies an index phenotype in a non-human index inbred strain comprising the steps of outcrossing BTBR mice to a B6-Min mouse, the B6-Min mouse carrying the Min allele at the murine Apc locus, which confers the phenotype of multiple intestinal neoplasia. Bilger *et al.* also teach backcrossing the B6-Min x BTBR mice to verify that the outlying phenotype is caused by a segregating mutation, and that BTBR mice carry a phenotype-modifying tumor susceptibility allele that confers greater susceptibility than any of the other crosses carried out, which could be considered an extreme outlying phenotype. Bilger *et al.* further teach crosses wherein the genetic background has a modifying effect on the index phenotype (reduces susceptibility to multiple intestinal neoplasia), and does not have a modifying effect on the index phenotype (does not reduce susceptibility to multiple intestinal neoplasia). In addition, the reference teaches mapping the location of the modifying allele (Mom-1) through multiple generations of backcrossing, and evaluating the progeny of the mapping cross (see, e.g., entire article, particularly page 251, column 2 through page 253, column 2).

Applicant's arguments filed 4/11/00 have been fully considered but they are not persuasive. It is argued that the teachings of Bilger *et al.* are merely background to the methods and products of the present invention. It is argued that in no instance does Bilger *et al.* describe crossing B6-*Min* mice either to mutagenized animals or to isogenic animals containing only random point mutations as recited in the claims (see page 10 of applicants' Response). This is not persuasive as applicants are arguing limitations not in the claims. There is no recitation of crossing B6-Min mice either to mutagenized animals or to isogenic animals containing only random point mutations. Thus, the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bilger *et al.* (of record) taken with Rinchik *et al.* (Proc. Natl. Acad. Sci. USA, 87:896-900, 1990, newly applied).

Bilger *et al.* teach a method for identifying a segregating mutation at a genetic locus that modifies an index phenotype in a non-human index inbred strain comprising the steps of outcrossing BTBR mice to a B6-Min mouse, the B6-Min mouse carrying the Min allele at the murine Apc locus, which confers the phenotype of multiple intestinal neoplasia. Bilger *et al.* also teach backcrossing the B6-Min x BTBR mice to verify that the outlying phenotype is caused by a segregating mutation, and that BTBR mice carry a phenotype-modifying tumor susceptibility allele that confers greater susceptibility than any of the other crosses carried out, which could be considered an extreme outlying phenotype. Bilger *et al.* further teach crosses wherein the genetic background has a modifying effect on the index phenotype (reduces susceptibility to multiple

intestinal neoplasia), and does not have a modifying effect on the index phenotype (does not reduce susceptibility to multiple intestinal neoplasia). In addition, the reference teaches mapping the location of the modifying allele (Mom-1) through multiple generations of backcrossing, and evaluating the progeny of the mapping cross (see, e.g., entire article, particularly page 251, column 2 through page 253, column 2).

Bilger *et al.* do not teach that the crosses employ preserved gametes. However, Cassou *et al.* teach a device for preserving gametes which can be subsequently used in *in vitro* fertilizations, etc. (see, e.g., column 1, lines 10-17 and 34-37). Although Cassou *et al.* do not disclose preservation of gametes obtained from genetic crosses, Rinchik *et al.* provide motivation for using preserved gametes due to the space limitations associated with generating progeny from crosses (see, e.g., page 897, right column).

It would have been obvious to one of ordinary skill in the art to employ preserved gametes, as taught by Cassou *et al.*, in a method for identifying a segregating mutation at a genetic locus that modifies an index phenotype in a non-human index inbred strain which requires numerous crosses and generates large numbers of progeny, as taught by Bilger *et al.* in view of the teachings of Rinchik *et al.* that progeny that are obtained from genetic crosses cannot be kept after weaning due to space limitations. Thus, it would have been obvious to store gametes from mice obtained different genetic crosses, rather than the mice as the preserved gametes can be used for subsequent fertilizations in genetic studies.

Thus the claimed invention is *prima facie* obvious especially in the absence of sufficient, clear, and convincing evidence to the contrary.

Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bilger *et al.* (of record) taken with Dietrich *et al.* (of record).

Bilger *et al.* teach a method for identifying a segregating mutation at a genetic locus that modifies an index phenotype in a non-human index inbred strain comprising the steps of outcrossing BTBR mice to a B6-Min mouse, the B6-Min mouse carrying the Min allele at the

murine Apc locus, which confers the phenotype of multiple intestinal neoplasia. Bilger *et al.* also teach backcrossing the B6-Min x BTBR mice to verify that the outlying phenotype is caused by a segregating mutation, and that BTBR mice carry a phenotype-modifying tumor susceptibility allele that confers greater susceptibility than any of the other crosses carried out, which could be considered an extreme outlying phenotype. Bilger *et al.* further teach crosses wherein the genetic background has a modifying effect on the index phenotype (reduces susceptibility to multiple intestinal neoplasia), and does not have a modifying effect on the index phenotype (does not reduce susceptibility to multiple intestinal neoplasia). In addition, the reference teaches mapping the location of the modifying allele (Mom-1) through multiple generations of backcrossing, and evaluating the progeny of the mapping cross (see, e.g., entire article, particularly page 251, column 2 through page 253, column 2).

Bilger *et al.* do not teach evaluating modified tumor multiplicity by determining the LOD score for the presence of the segregating mutation. However, Dietrich *et al.* teach the use of LOD scores for evaluating the presence of segregating mutations (see, e.g., page 633, left column and pages 637-638, under "Genotype Analysis").

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Bilger *et al.* by obtaining a LOD score for statistically evaluating the presence of segregating mutations observed in the crosses as this evaluation method is well known in the art and has been used in the genetic identification of a major modifier locus affecting Min-induced intestinal neoplasia in mice, as taught by Dietrich *et al.*

Thus the claimed invention is *prima facie* obvious especially in the absence of sufficient, clear, and convincing evidence to the contrary.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet M. Kerr whose telephone number is (703) 305-4055. Should the

examiner be unavailable, inquiries should be directed to Deborah Clark, Supervisory Primary Examiner of Art Unit 1633, at (703) 305-4051. Any administrative or procedural questions should be directed to Kimberly Davis, Patent Analyst, at (703) 305-3015. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 305-7401.

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